35 Protective effect of superoxid dismutase (SOD) on severe lung damage caused by xanthine oxidase (XO).

O.D.SAUGSTAD, M.HALLMAN, G.BECHER*, A. ODDOY*, B. LACHMANN*.
Dept.of Paed.,The National Hospital of Norway, Oslo,Childrens Hospital,Helsinki and Research Institute for lung diseases, Berlin-Buch,GDR.

During post hypoxic resuscitation the hypoxanthine-xanthine oxidase system creates free oxygen radicals. The effect of free oxygen radicals on the lungs were studied by applying 1 U XO into the trachea of guinea pigs. Lung compliance and arterial blood gases were monitored. Compliance and PaO_2 decreased ($p<0.01$) after application of XO in 1 ml saline (3 ml/kg), when compared with saline alone. SOD (20000 U) prevented the effect of XO. When ventilating with a peak pressure of 20 cm H_2O 20 minutes after application of the fluid the data were:

	XO	NaCl	XO+SOD	SOD	untreated
Compliance	0.13	0.27	0.24	0.30	1.00
ml/cm H_2O.kg	±0.07	0.11	0.06	0.10	0.20
paO_2	10.8	13.7	14.4	13.7	16.4
kPa	± 2.4	1.9	2.1	2.1	0.9

The data demonstrate that XO potently damages the lungs probably through O_2- formation since SOD prevents the effect. The SOD effect lasts about one hour. The data also show that there is a dramatic effect on healthy lungs when saline is applied into the trachea. This raises the question whether randomised studies for surfactant treatment are justified.

36 NEURAL TUBE DEFECTS (NTD): FAMILY STUDIES. Jacek J. Pietrzyk, Bogdan Rozanski 1st Department of Pediatrics, Institute of Pediatrics, Krakow, Poland.

A population of 360 families, with at least one child with anencephaly and/or myelomeningocele or encephalomeningocele was ascertained by multiple selection in the Southern Poland where the birth prevalence of NTD is 0.89/1000. The probability of ascertainment π equalled 0.64. The population birth prevalence of NTD and the prevalence of NTD among the probands' sibs were used to calculate the relative risk and heritability. Complex segregation analysis by the method of maximum likelihood was applied in an attempt to discriminate between the hypotheses of single locus and that of quasi-continuity under multifactorial inheritance. A special program YUKONS in FORTRAN for Cyber 72 CDC computer was preapred. The recurrence risk of NTD among the probands' sibs was 3.4% ± 1.6, being about 39 times (χ^2 = 181.31 $p < 0.0005$) the population prevalence at birth. The heritability calculated on the regression of siblings on propositi was 76% ± 7. The results of complex segregation analysis excluded the hypothesis of multifactorial inheritance (χ^2 = 18.186 df=46). The hypotheses of two allele model at a single autosomal locus fit the data with much better degree of exactness. Among the eight hypotheses the best conformity (χ^2 = 9.375 df=45) was observed for additive model (d = 0.5) with penetrance t=0.605 and frequency of phenocopies x = 0.546. These results suggest that major additive genes might be responsible for NTD inheritance.

37 STUDY ON PATHOGENESIS OF RESPIRATORY FAILURE IN ACUTE LUNG INJURY. B. LACHMANN*, M. HALLMAN. Childrens´ Hospital, Univ. Helsinki, Finland, and Instit. Lung Diseases, Berlin, DDR.

Respiratory distress syndrome in the newborn resembles acute severe respiratory failure (ARF). ARF is associated with a number of ethiologies that cause diffuse lung injury. Hyperimmune rabbit serum against guinea pig lung proteins (ALS) induces acute fatal respiratory failure similar to ARF (Pädiatrie 14, 211,1975). We have studied movement of molecules in and out of the airways within 30 min after intravenous ALS. Guinea pigs that received saline or normal rabbit serum served as controls. ^{131}I-Albumin and ^{14}C,^{3}H-labeled surfactant were injected either intravenously or intratracheally prior to ALS. Following ALS the airways became freely permeable to albumin. Despite effective mechanical ventilation the airways became flooded with protein. Within 30 min 26% (control 0.5%) of the intravenous ^{131}I-albumin was recovered from the airways. More than 80% of intravenous surfactant was cleared from circulation but only 0.5% (control 0.02%) of it entered the airways. Lavageable surfactant pool decreased by 40% within 30 min after ALS. More than 95% of the complex that left the airways was recovered in the residual lung. Bronchial surfactant was inactivated by proteins and glycolipids that entered the airways after ALS.

We have demonstrated a severe surfactant defect within 30 min after acute lung injury. We have also shown that the survival and lung function can be improved by surfactant substitution after ALS. Therefore we propose that surfactant deficiency plays a central role in early pathogenesis of ARF.

38 SURFACTANT SUBSTITUTION IN RDS. AN EVALUATION OF THE TURNOVER OF EXOGENEOUS AND ENDOGENEOUS SURFACTANT. M. HALLMAN, T.A. MERRITT*, L.GLUCK*. Childrens Hospital, Univ. Helsinki, Finland, and Dept. Pediatrics, Univ. California, San Diego.

A potential side effect of exogeneous surfactant is inhibition of the endogeneous surfactant secretion. We have studied this question. Human surfactant (HS, 120 mg/kg) was given before the age of 10 h, in order to treat severe RDS. Tracheal aspirates (N=128) were recovered from ten infants (BW 1013±285 g; GA 27.4±1.1 w; 5 received HS, 5 controls) and analyzed for phospholipids. The interpretation of the results is based upon the following knowledge: 1. In tracheal aspirate the phospholipid composition is similar to that in alveolar lavage. 2. Surfactant phospholipids from RDS and from no-RDS are similar except for the acidic phospholipids: in RDS there is only phosphatidylinositol (PI), whereas normal surfactant contains both PI and phosphatidylglycerol (PG). 3. The high serum myoinositol in RDS prevents PG synthesis (J.Clin.Invest. 68, 742,1981).

The turnover of exogeneous HS was measured on the basis of the exponential decay data of PG/(PG+PI)-ratio. The half-life of PG was 33±5 h. HS substitution increased HS pool size 5-22-fold, and increased saturated lecithin/sphingomyelin (L/S) from 3.0±0.4 to 25.0±8.3. Subsequently L/S remained high and the respiratory status improved. At the age of one week the treated infants had higher L/S than the controls (22.4±3.7 vs 9.4±1.7). According to present evidence exogeneous HS did not suppress endogeneous HS secretion. Instead, exogeneous HS may be utilized for endogeneous synthesis of surfactant.

39 Transfusion acquired cytomegalovirus infection in the preterm infant.

DECATES CR*, WALKER J*, GRAY J*,NAGINGTON J*, ROBERTON NRC. Addenbrooke's Hospital, Departments of Paediatrics and Public Health, Hills Road, Cambridge.

In order to evaluate the risk to very premature infants of acquiring cytomegalovirus (CMV) infection from blood transfusion, a prospective study of 70 babies of 32 weeks gestation or less, who received transfusions of unscreened blood was undertaken. Specimens of cord blood, postnatal maternal blood and babies blood at approximately one month post term were tested by complement fixation test for CMV.IgG antibodies and where indicated by radioimmunoassay for CMV specific IgM. Urine specimens from babies and mothers, taken shortly after delivery and from babies at follow up were cultured by routine methods for CMV. Aliquots of the blood used to transfuse the babies were tested retrospectively for antibodies to CMV. Clinical details, methods of feeding and progress on follow up were recorded. Ten babies acquired CMV infection postnatally. Three babies were thought to have transfusion acquired CMV infection, and one died as a result. No other baby had obvious clinical sequelae. Two infections were definitely not transfusion related, and of the remaining five, one occurred in a baby born to a mother with acute CMV hepatitis and four were probably acquired after discharge from hospital, possibly from infected breast milk. Premature babies are at risk from transfusion acquired CMV infection, but other sources of infection, notably unpasteurised breast milk from seropositive mothers and milk banks should be considered.

40 Insulin secretion is linearly proportional to blood glucose in insulin dependent diabetes (IDDM)

JOHNNY LUDVIGSSON*
Dept of Pediatrics,Univ Hospital,Linköping, Sweden

Low insulin in IDDM may depend on a defect insulin-release process and/or decreased number of beta cells. The aim of this study was to elucidate this question by analysing how the insulin secretion is related to actual blood glucose.

Patients and methods: Blood samples were drawn at day 0, 3,30,90,180,270,540 from 28 children who got IDDM at the age of 4-15 yrs (mean±SD 9.8±3.3). At 90, 270, 540 days a standardized breakfast was given and blood drawn after 0,30,60,90,120 min. C-peptide and blood glucose were determined.

Results: At diagnosis C-peptide was detectable in all children(range 0.05-0.58 pmol/ml;mean±SD 0.21±0.13). Fasting values reached a maximum at 3 months duration (0.04-0.58;0.21±0.11) as well as maximal C-peptide response (0.08-0.80;0.43±0.21). The cross-sectional correlation between blood glucose and C-peptide was weak, but in the individual patients the C-peptide response to breakfast was linearly correlated to the blood glucose increase still up to blood glucose values high above normal(at 3 months r=0.98,at 9 months r=0.97 and at 18 months r=0.98). Insulin secretion started at the same glucose but a certain C-peptide increase was associated with higher blood glucose at 18 than at 9 and 3 months.

Conclusion: The results indicate that the relationship between blood glucose and insulin secretion after breakfast is normal in children with IDDM. This suggests that the low insulin release mainly depends on too few beta cells.